## REMARKS

### Status of the Claims

Claims 1-13, 18-29 and 32-34 are currently pending in this application. Claims 14-17, 30-31 and 35-36 were previously canceled. In this amendment, claim 1 is amended and claims 32-34 are canceled without prejudice or disclaimer. Support for the amendment may be found throughout the specification as filed, for example, at page 1, lines 19-20; page 12, lines 24-25; page 17, lines 21-22; and in Examples 1, 2 and 4 (page 20, lines 6-7; page 21, lines 5-7; and page 22, lines 6-8). No new matter has been added. Upon entry of the amendment, claims 1-13 and 18-29 will be pending. Entry of the amendment and reconsideration in view of the following comments are respectfully requested.

With respect to all amendments, Applicants have not dedicated or abandoned any unclaimed subject matter and have not acquiesced to any rejections and/or objections made by the Patent Office. Applicants expressly reserve the right to pursue prosecution of any presently excluded subject matter or claim embodiments in one or more future continuation and/or divisional application(s).

### Information Disclosure Statements

Applicants appreciate the Examiner's consideration of materials listed in the Information Disclosure Statements submitted on May 15, 2008 and August 12, 2008.

### Rejection Under 35 U.S.C. § 102

*Anticipation by Dzieglewska*

Claims 1-6, 11-13, 18-25, 27-28 and 32-34 are rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Dzieglewska *et al.* (WO98/51693, hereinafter "Dzieglewska"), which teaches a method of isolating and amplifying nucleic acids of interest from a cell sample using, *inter alia*, magnetic beads. Applicants respectfully traverse this rejection for the reasons set forth below.

The legal standard for anticipation under 35 U.S.C. § 102 is one of strict identity. *Trintec Industries, Inc. v. Top-U.S.A. Corp.*, 63 U.S.P.Q.2d 1597 (Fed. Cir. 2002). To anticipate a claim, a single prior source must contain each and every limitation of the claimed invention. *In re Paulson*, 30 F.3d 1475, 1478-79, 31 USPQ2d 1671, 1673 (Fed. Cir. 1994) (citing *In re Spada*, 911 F.2d 705, 708, 15 USPQ2d 1655, 1657 (Fed. Cir. 1990)). "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987); MPEP §2131.

As a preliminary matter, claim 1 has been amended to recite the following limitation: "wherein said process does not comprise a step of lysing said target cell or virus to release said nucleic acid prior to applying said separated conjugate to said nucleic acid amplification system." As indicated above, support for this amendment may be found in the specification as filed, for example, at page 1, lines 19-20; page 12, lines 24-25; page 17, lines 21-22; and in Examples 1, 2 and 4 (page 20, lines 6-7; page 21, lines 5-7; and page 22, lines 6-8). Each of claims 2-13 and 18-29 depends, directly or indirectly, from claim 1 and therefore incorporates all of its limitations. Claims 32-34 have been canceled, thereby rendering all comments directed to these claims moot.

Dzieglewska teaches a method of isolating nucleic acid from a sample of cells comprising: (a) binding cells in the sample to a solid supports to isolate cells from the sample; (b) lysing the isolated cells to release nucleic acid; and (c) binding nucleic acid released from the lysed cells to the same solid support (abstract; page 4, lines 15-22; emphasis added). Dzieglewska expressly teaches that "[f]ollowing cell binding, the isolated or support-bound cells are lysed to release their nucleic acid" (page 11, lines 14-15) and discloses a wide variety of cell lysis methods on page 11, line 16 through page 13, line 11. Dzieglewska does not contain any teaching, express or implied, for a method of nucleic acid amplification that does not comprise lysing the target cell or virus to release the nucleic acid prior to amplification, as required by the presently amended claim 1. Since Dzieglewska fails to teach each and every element of claim 1 and claims depending therefrom, the strict identity standard of anticipation under 35 U.S.C. § 102 is not satisfied. Accordingly,

Applicants respectfully submit that this rejection under 35 U.S.C. § 102(b) may properly be withdrawn.

**Rejections Under 35 U.S.C. § 103**

*Dzieglewska in View of Ughelstad*

Claims 7-10 are rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Dzieglewska as applied to claims 1-6, 11-13, 18-25, 27-28 and 33-34 above and further in view of Ughelstad *et al.* (WO83/03920, hereinafter "Ughelstad"), which teaches a process for making magnetic particles. The Examiner asserts that it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to have applied the teachings of Ughelstad to the particles of Dzieglewska to arrive at the claimed invention with a reasonable expectation for success. Applicants respectfully traverse this rejection for the reasons set forth below.

The Examiner bears the burden of establishing a *prima facie* case of obviousness. *In re Rijckaert*, 9 F.3d 1531, 1532 (Fed. Cir. 1993). The obviousness analysis under 35 U.S.C. § 103(a) requires the consideration of the scope and content of the prior art, the level of skill in the relevant art, and the differences between the prior art and the claimed subject matter must be considered. *KSR Int'l Co. v. Teleflex Inc.*, 127 S.Ct. 1727 (2007) (citing *Graham v. John Deere Co.*, 383 U.S. 1, 17 (1966)). To establish a *prima facie* case of obviousness a three-prong test must be met. First, the prior art must reference must teach or suggest all the claim limitations. *In re Royka*, 490 F.2d 981, 985 (CCPA 1974). Second, there must be some suggestion or motivation, either in the references or in the knowledge generally available among those of ordinary skill in the art, to modify the reference to achieve the claimed invention. *KSR* at 1731. And third, there must be a reasonable expectation of success found in the prior art. *In re Vaeck*, 947 F.2d 488 (Fed. Cir. 1991).

Rejections on obviousness grounds cannot be sustained by mere conclusory statements. *In re Kahn*, 441 F.3d 977, 987-88 (Fed. Cir. 2007) (citations omitted). Critical elements of the invention as a whole which clearly distinguish the entire invention from the prior art references cannot be ignored. *Panduit Corp. v. Dennison Manufacturing Co.*, 1 U.S.P.Q.2d 1593, 1597 (Fed. Cir.), *cert. denied*, 481 U.S. 1052 (1987). Evidence of an unobvious or unexpected advantageous

property can rebut prima facie obviousness. MPEP § 716.02(a). Moreover, if a proposed modification changes the principle of operation of a reference, the teachings of that reference are not sufficient to render the claimed invention obvious. MPEP § 2143.01.VI, citing *In re Ratti*, 270 F.2d 810, 123 USPQ 349 (CCPA 1959) (emphasis added).

The teachings of Dzieglewska and the current amendment to claim 1, from which each of claims 7-10 depends, are discussed above. Ughelstad teaches a method of making magnetic polymer particles by treating compact or porous polymer particles with a solution of iron salts and, optionally, salts of other metals which are capable of forming magnetic ferrites (*e.g.*, $Mn^{2+}$, $Co^{2+}$ or $Ni^{2+}$), wherein the solution swells or penetrates into the particles. Much like Dzieglewska, Ughelstad does not teach or even suggest a method of nucleic acid amplification that does not comprise lysing the target cell or virus to release the nucleic acid prior to amplification, as required by the presently amended claim 1. Moreover, since the present invention has a different principle of operation than the one disclosed in the cited references, the teachings of these references are clearly insufficient to render the present invention obvious under *In re Ratti*.

Thus, neither of the cited references, alone or in combination, teaches or suggests a method of nucleic acid amplification that does not comprise lysing the target cell or virus to release the nucleic acid prior to amplification. In the absence of a teaching or suggestion of each and every claim element, the cited combination fails to provide the motivation to practice the presently claimed invention. Accordingly, Applicants respectfully submit that the Examiner has failed to establish a *prima facie* case of obviousness, and this rejection under 35 U.S.C. § 103(a) may properly be withdrawn.

*Dzieglewska in View of Inuma*

Claim 26 is rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Dzieglewska as applied to claims 1-6, 11-13, 18-25, 27-28 and 33-34 and further in view of Inuma *et al.* (*Int. J. Cancer* 2000, 89:337-344, hereinafter "Inuma"), which teaches that leukocytes can be specifically targeted by magnetic beads having antibodies immobilized thereon. The Examiner asserts that it would have been *prima facie* obvious to one of ordinary skill in the art at the time of

the invention to have analyzed the target cells of Inuma using the method of separation taught by Dzieglewska to arrive at the claimed invention with a reasonable expectation for success. Applicants respectfully traverse this rejection for the reasons set forth below.

The teachings of Dzieglewska and the current amendment to claim 1, from which claim 26 depends, are discussed above. Inuma teaches highly specific separation of $CD45^+$ cells using magnetic microbeads coated with anti-CD45 antibodies (page 338, emphasis added). Much like Dzieglewska, Inuma does not teach or even suggest a method of nucleic acid amplification that does not comprise lysing the target cell or virus to release the nucleic acid prior to amplification, as required by the presently amended claim 1. Moreover, since the present invention has a different principle of operation than the one disclosed in the cited references, the teachings of these references are clearly insufficient to render the present invention obvious under *In re Ratti*.

Thus, neither of the cited references, alone or in combination, teaches or suggests a method of nucleic acid amplification that does not comprise lysing the target cell or virus to release the nucleic acid prior to amplification. In the absence of a teaching or suggestion of each and every claim element, the cited combination fails to provide the motivation to practice the presently claimed invention. Accordingly, Applicants respectfully submit that the Examiner has failed to establish a *prima facie* case of obviousness, and this rejection under 35 U.S.C. § 103(a) may properly be withdrawn.

*Dzieglewska in View of Lopez-Sabater*

Claim 29 is rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Dzieglewska as applied to claims 1-6, 11-13, 18-25, 27-28 and 33-34 above, and further in view of Lopez-Sabater *et al.* (*Lett. Appl. Microbiol.* 1997, 24:101-104; hereinafter "Lopez-Sabater"), which teaches a method for the magnetic immunoseparation for detection of viral sequences by PCR. The Examiner asserts that it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to have combined the technique of homogenization of a sample suspected of containing a virus as taught by Lopez-Sabater with the method of isolation and analysis taught by

Dzieglewska to arrive at the claimed invention with a reasonable expectation for success. Applicants respectfully traverse this rejection for the reasons set forth below.

The teachings of Dzieglewska and the current amendment to claim 1, from which claim 29 depends, are discussed above. Lopez-Sabater teaches the use of Streptavidin MagneSphere® Paramagnetic beads (Promega) coated with biotinylated human anti-HAV (Hepatitis A virus) IgG for virus capture and the removal of the RT-PCR inhibitory compounds that are often present in a shellfish extract. Much like Dzieglewska, Lopez-Sabater does not teach or even suggest a method of nucleic acid amplification that does not comprise lysing the target cell or virus to release the nucleic acid prior to amplification, as required by the presently amended claim 1. Moreover, since the present invention has a different principle of operation than the one disclosed in the cited references, the teachings of these references are clearly insufficient to render the present invention obvious under *In re Ratti*.

Thus, neither of the cited references, alone or in combination, teaches or suggests a method of nucleic acid amplification that does not comprise lysing the target cell or virus to release the nucleic acid prior to amplification. In the absence of a teaching or suggestion of each and every claim element, the cited combination fails to provide the motivation to practice the presently claimed invention. Accordingly, Applicants respectfully submit that the Examiner has failed to establish a *prima facie* case of obviousness, and this rejection under 35 U.S.C. § 103(a) may properly be withdrawn.

## CONCLUSION

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejection of the claims and to pass this application to issue. If it is determined that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the event the U.S. Patent and Trademark office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing **docket No. 514572000700**. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

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